The rationale for perioperative bridging is anchored on mitigating the risk of major cardiovascular events, including stent thrombosis, in patients who require surgery and in whom the associated risk of bridging-related bleeding is acceptably low. A number of agents, including unfractionated heparin, low-molecular-weight heparins, glycoprotein IIb/IIIa antagonists, direct thrombin inhibitors (bivalirudin), and reversible platelet P2Y<sub>12</sub>-receptor inhibitors, have been proposed and studied as bridging agents.

We recognize the foundational work at The Geelong Hospital and that carried out by Savonitto et al<sup>1</sup> and Bolsin et al. These case reports and observational studies provide the impetus and rationale for future study in this area. Further encouraging evidence comes from a recent randomized, placebo-controlled trial of 210 patients with acute coronary syndromes or treated with a coronary stent on a thienopyridine, awaiting coronary artery bypass grafting. In this study, patients received IV cangrelor, a short-acting, reversible P2Y<sub>12</sub>-receptor inhibitor, or placebo for at least 48 h, which was stopped 1 to 6 h before surgery. Patients in the cangrelor group had lower levels of platelet reactivity with no significant increase in coronary artery bypass grafting-related bleeding.<sup>5</sup> Whether this agent can be used safely in the noncardiac surgery setting has yet to be determined.

The current evidence points toward a lack of consensus regarding best practices for patients with coronary stents undergoing noncardiac surgery. This is particularly true for bridging strategies, where the majority of guidelines provide no recommendations. Well-designed prospective observational and randomized trial evidence is needed to help define future management strategies.

Saeed Darvish-Kazem, MD
James D. Douketis, MD, FCCP
Hamilton, ON, Canada

**Affiliations:** From the Department of Medicine (Dr Darvish-Kazem and Douketis), Michael G. DeGroot School of Medicine (Dr Douketis), McMaster University; and St. Joseph’s Healthcare Hamilton (Dr Douketis).

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**Correspondence to:** James D. Douketis, MD, FCCP, St. Joseph’s Healthcare Hamilton, Room F-544, 50 Charlton Ave E, Hamilton, ON, L8N 4G6, Canada; e-mail: jdouket@mcmaster.ca

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**Adrenal Suppression With Mometasone Furoate/Formoterol**

To the Editor:

I read with interest the article by Kosoglu et al (December 2013) comparing the relative adrenal suppression of mometasone furoate/formoterol (MF/F) vs fluticasone propionate/salmeterol (FP/S) combination inhalers via metered-dose inhalers in patients with mild to moderate asthma. The geometric mean ratio for cortisol area under curve (AUC) comparing MF/F 400/10 μg bid (n = 15) vs FP/S 460/42 μg bid (n = 16) was 1.19 (90% CI, 1.01-1.40), which, although falling within predefined ± 30% equivalence limits (ie, corresponding to a ratio of 0.70-1.43), clearly represents a significant difference, as the lower CI exceeds unity, indicating that FP produces greater adrenal suppression than MF when used at higher doses. Indeed, the individual data in Figure 1 in their article<sup>1</sup> appear to show more uniform adrenal suppression for FP/S 460/42 μg bid, with all but one subject exhibiting abnormal values less than unity for the ratio of cortisol AUC relative to baseline. Although the geometric mean ratio for AUC cortisol for MF/F 200/10 μg bid (n = 13) was not significantly different from placebo (n = 16; 0.92 [90% CI, 0.78-1.10]), this could merely be due to type 2 error. Pointedly, there was no mention of any a priori power calculations. Moreover, for such pharmacodynamic end points it is more conventional to report 95% CI rather than 90% CI. On inspecting Figure 1,<sup>1</sup> it appears that, for the ratio of cortisol AUC relative to baseline, there are only two of 16 individuals (13%) with abnormal values less than unity for placebo, vs seven of 13 (54%) for MF/F 200/10 μg bid. It is unclear if patients were washed out of their usual inhaled corticosteroid therapy prior to randomization, since they may already have exhibited a degree of adrenal suppression at baseline, which in turn would attenuate the ratio of subsequent suppression relative to baseline.

Since the lung bioavailability of MF/F is essentially determined by lung deposition, it would be informative to know the respective in vitro fine particle dose and particle size for each dose formulation of MF/F and how this compares to FP/S.<sup>2</sup> It can be seen from pharmacokinetic data that the accumulation ratio between single and chronic dosing for the MF moiety is appreciable, being 2.64-fold at 200 and 4.46-fold at 2000 μg bid. It is unclear if patients were washed out of their usual inhaled corticosteroid therapy prior to randomization, since they may already have exhibited a degree of adrenal suppression at baseline, which in turn would attenuate the ratio of subsequent suppression relative to baseline.

The mean baseline FEV<sub>1</sub> % predicted is not reported for each group either at baseline or while taking randomized treatments, which is important to know, because airway caliber will determine the degree of lung absorption of inhaled corticosteroid and, hence, its degree of systemic bioactivity<sup>4</sup>; for example, patients with an FEV<sub>1</sub> of 60% predicted would be expected to absorb less MF than those with 90% predicted and, hence, produce less adrenal suppression. Furthermore, if the FEV<sub>1</sub> % ended up being higher while taking formoterol or salmeterol, this might augment the relative degree of lung bioavailability from the MF or FP moieties, respectively. Finally, the authors omit to mention that using either of these combination inhalers through a spacer device would approximately double their relative lung bioavailability and associated degree of adrenal suppression.<sup>5</sup> The data of Kosoglu et al<sup>1</sup> serve to reinforce the importance of always stepping down to achieve...
the lowest possible maintenance dose of inhaled corticosteroid to achieve the least potential for long-term systemic exposure in a given individual patient.

Brian J. Lipworth, MD
Dundee, Scotland

Affiliations: From the Asthma and Allergy Research Group, Medical Research Institute, Ninewells Hospital and Medical School, University of Dundee.

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Correspondence to: Brian J. Lipworth, MD, Asthma and Allergy Research Group, Medical Research Institute, Ninewells Hospital and Medical School, University of Dundee, Dundee, DD1 9SY, Scotland; e-mail: b.j.lipworth@dundee.ac.uk

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Another Rare Finding of Lymphomatoid Granulomatosis on CT Scan

To the Editors:

We thank Hadid et al1 for their article in CHEST (January 2014). The authors wrote an excellent case report concerning a lung mass subsequently diagnosed as lymphomatoid granulomatosis (LYG). The authors reported that common findings on CT scan are peribronchovascular distribution of nodules, coarse irregular opacities, small thin-wall cysts, small nodules, and, rarely, a mass, as presented in this case.

We would like to share two other findings on CT scan in LYG, including reversed halo sign2 and air crescent sign.3 The reversed halo sign is a focal round area of ground-glass attenuation and surrounding airspace consolidation of crescent shape that is more commonly seen in cryptogenic organizing pneumonia.2 The air crescent sign is crescentic and radiolucent due to a lung cavity that is filled with air and has a round radiopaque mass that is most commonly found in pulmonary aspergillosis.3 Diagnosis of LYG is often a challenge, as it mimics many other more common pulmonary conditions, and, therefore, the histologic triad of polymorphic lymphocytic infiltrate, angiitis, and granulomatosis with central necrosis is required for definitive diagnosis.7

Narat Srivali, MD
Cooperstown, NY
Patompong Ungprasert, MD
Cooperstown, NY

Affiliations: From the Department of Medicine (Drs Srivali and Ungprasert), Bassett Medical Center; and Department of Medicine (Dr Jariyawat), Ramathibodi Hospital. Financial/nonfinancial disclosures: The authors have reported to CHEST that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

Correspondence to: Narat Srivali, MD, Bassett Medical Center, Medicine, One Atwell Rd, Cooperstown, NY 13326; e-mail: narat.srivali@bassett.org

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Response

To the Editor:

We thank Dr Srivali and colleagues for their letter regarding our case report.1 We appreciate their added contribution of two other CT scan findings that are more commonly seen in other disease processes and reiterate the important point that diagnosis of lymphomatoid granulomatosis (LYG) often is a challenge and confirm that there are no specific radiologic findings of LYG. We would like to note that despite the nomenclature, granulomas are not a histologic feature of this entity. The hallmark of LYG is a mixed mononuclear cell infiltrate containing large, variably atypical B cells and small T cells, often along with plasma cells and histiocytes, which replaces the lung parenchyma and shows vascular infiltration.